SCCG News

SENIOR CARE CONSULTANT GROUP

Consultant Pharmacists...Dispensing Knowledge

www.mySCCG.com

December, 2011

INSIDE THIS ISSUE:

The Problem With Drug Shortages

Drug shortages in the United States have been on the rise. The FDA recognizes the significant public health consequences that can result from drug shortages and makes tremendous efforts within its legal authority to address and prevent drug shortages.

The drugs in shortage are constantly changing, but in general the main types of drugs that have been in shortage have involved cancer drugs, anesthetics used for patients undergoing surgery, sterile injectable drugs, electrolytes used for patients needing intravenous nutrition therapy, and other medically necessary sterile drugs.

FDA initiated the Drug Shortages Program in 1999 and has been tracking numbers of shortages annually since 2005. During this time period, we have noted a steady increase in shortages. In 2010, there was a record number of shortages, and in 2011 FDA has continued to see an increasing number of shortages, especially those involving older sterile injectable drugs.

There are a number of different factors contributing to the current shortage of sterile injectables and other drugs, including manufacturing issues and economic factors. Some companies have decided to discontinue making their products for business reasons, others have had problems with their raw-material suppliers, and some have experienced manufacturing deficiencies that compromise the safety and efficacy of their products.

In 2010, a majority of the drugs in shortage had quality and manufacturing problems. Some of these quality problems included the presence of particulates, microbial contamination, and newly identified impurities in sterile injectables. Companies sometimes voluntarily stop production or suspend production of critical drugs when manufacturing problems occur so that they can resolve the root cause of product-quality problems. Some of these issues are complex, and companies may need to take substantial amounts of time to correct the underlying cause of the problem.

When a company identifies a quality problem, it will often try to address the problem while still continuing to manufacture the product. FDA works closely with companies to ensure that appropriate corrective actions are implemented in a timely manner, without interrupting the supply of medically necessary drug products, while also ensuring that the products produced are safe and effective. However, there are times when a company decides that it must recall or stop manufacturing a product. FDA works with the company to address the issues. Problems may be very low risk (eg, wrong expiration date on package) to high risk (particulate in product or sterility issues). FDA will look at the risk-benefit balance on a case-by-case basis in order to be flexible in addressing shortages and to mitigate any risk to patients.

FDA also works with other companies making the drugs that are in shortage to help them ramp up production if they are willing to do so. Often they need new production lines or new raw material sources approved to help increase supplies. FDA can and does expedite review of these to help resolve shortages of medically necessary drugs. However, FDA can't *require* the other companies to increase production.

When a shortage occurs and a company has inventory that is close to expiry or already expired, extension of the expiration dating for that inventory can be considered if the company has data to support that extension. In those situations, FDA is able to review this data and approve the extended dating to help increase supplies until new production is available.

Continued on Page 4

Low-Dose Intradermal Flu Vaccine Effective as Intramuscular

Injecting a lower dose of 2010/11 trivalent influenza vaccine (TIV) intradermally was more immunogenic than a traditional full-dose intramuscular injection for chronically adults, Ivan Hung, MD, clinical assistant professor in the Department of Medicine at the University of Hong Kong, China, reported here at the Infectious Diseases Society of America (IDSA) 49th Annual Meeting. Dr. Hung and colleagues used 1 of 2 devices to administer intradermal injections using 20% or 60% of the standard dose, and compared the immunogenicity with standard doses delivered intramuscularly in an open-label, prospective, randomized trial.

From December 2010 to March 2011, 282 chronically ill adults were randomly assigned to 1 of 4 treatments: TIV containing 3 ì g of hemagglutinin antigen per strain, administered with a MicronJet600 device; the same treatment but with 9 ì g of hemagglutinin antigen per strain; 9 ì g of Intanza9 vaccine, administered with the Soluvia device (Sanofi-Aventis); and 15 ì g of TIV administered intramuscularly (control group). Immunogenicity was determined through a hemagglutination inhibition assay at baseline and 21 days after vaccination.Of the 282 subjects enrolled, 262 completed the study — approximately evenly divided among the 4 groups (63 to 68 per group.) Demographically, the groups were similar, with a median age of 73.5 years (range, 68.0 to 78.5 years).

In all cases, seroconversion, seroprotection, and geometric mean titer fold increases were at least as good or better for the intradermal groups than for the intramuscular group in terms of response to the A/H1N1, H3N2, and influenza B components of the vaccines. "The reason for that is perhaps [because] the intradermal vaccination attracted dendritic cells, and that actually mounted a much better immune response," Dr. Hung said, also noting that no serious adverse effects were detected.

He recommends that all elderly and immunocompromised individuals receive intradermal influenza immunizations to compensate for their reduced reactivity to vaccines.

"Intradermal vaccination actually mounted a much better immune response, and that would offer better protection against influenza and the complications of influenza (for example, pneumonia) in the elderly population and also for those immunocompromised hosts," Dr. Hung told *Medscape Medical News*. "For the lower dose, you have slightly fewer side effects in terms of swelling, in terms of redness, which is important for elderly people and perhaps has less systemic effects. "He explained that intradermal injection is quite easy to give, and suggested that intradermal dose reduction might be an effective way to make vaccine go further in situations of high demand during future pandemics, once the efficacy of dose-sparing vaccination in healthy individuals has been demonstrated.

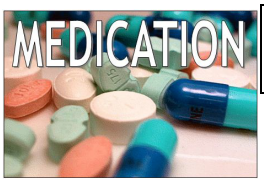
Andrew Pavia, MD, chief of pediatric infectious disease at the University of Utah, Salt Lake City, and chair of the Pandemic Influenza Task Force of the IDSA, who was not involved in the study, told *Medscape Medical News* that it is worthwhile investigating better ways for influenza immunization. "The weakness of flu vaccine is that it doesn't cause as good an antibody response in the elderly. One of the things that we'd like to do is to get a flu vaccine or a way of delivering the old flu vaccine that works just as well in the frail elderly as it does in healthy young and middle-aged adults."

Besides the equivalent or better efficacy that Dr. Hung showed, Dr. Pavia sees other advantages of intradermal injections. "There have been reports that with intradermal devices, it hurts much less going in because the needle is a microneedle, which people barely feel, but there may be increased itching or redness at the site, compared to getting a deeper injection with an intramuscular vaccine.

Some people may prefer itching to injection pain," he said. "The efficacy studies really haven't been done to show that they're truly equivalent. Cost would be the only other barrier. I think as an alternative, this is very interesting and potentially very useful."

He also sees intradermal injection as an advantage for people who are "relatively needle-phobic." "It may be useful when you've got a less-skilled population because this is pretty much an automatic device — you don't have to be skilled in giving an intramuscular injection, and of course, there's less risk of needle sticks," he explained.

Source: Daniel M. Keller, PhD; Medscape.com



UPDATE

The U.S. Food and Drug Administration today approved **Arcapta Neohaler** (indacaterol inhalation powder) for the long term, once-daily maintenance bronchodilator treatment of airflow obstruction in people with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and/or emphysema.

COPD is a serious lung disease that makes breathing difficult. Symptoms can include breathlessness, chronic cough and excessive phlegm. Cigarette smoking is the leading cause of COPD, and is the fourth leading cause of death in the United States, according to the Centers for Disease Control and Prevention.

Arcapta Neohaler is a new molecular entity in the beta2-adrenergic agonist class that helps muscles around the airways of the lungs stay relaxed to prevent symptoms of COPD, such as wheezing and breathlessness. Arcapta Neohaler is not intended to treat asthma or sudden, severe symptoms of COPD.

"The approval of new long-term drugs for COPD that relieve breathing difficulty by opening airways provides another treatment option for the millions of people," said Curtis Rosebraugh, M.D., M.P.H., director of the Office of Drug Evaluation II in the FDA's Center for Drug Evaluation and Research.

The safety and efficacy of Arcapta Neohaler was demonstrated in six confirmatory clinical trials that included 5,474 patients ages 40 and older with a clinical diagnosis of COPD. Those treated had a smoking history of at least one pack a day for 10 years and exhibited moderate-to-severe decreases in lung function.Arcapta Neohaler carries a boxed warning that long-acting beta2 adrenergic agonists (LABA) increase the risk of asthma-related death. All LABA, including Arcapta Neohaler, should not be used in patients with asthma, unless used with a long-term asthma control medication. The FDA approved Arcapta Neohaler with a medication guide that includes instructions for use and information about the potential risks of taking the drug. The most common side effects reported by those using Arcapta Neohaler include runny nose, cough, sore throat, headache and nausea.

Source: FDS.gov

VS. TRUTH

RUMOR: SSRIs are more dangerous than tricyclic antidepressants in elderly patients.

TRUTH: More research is necessary to answer the question of comparative safety. When an antidepressant is recommended for an older patient, side effects should be considered, such as, drug-disease interactions, drug-drug interactions, patient preferences, financial and formulary considerations, and other medical problems. Antidepressants should always start low and go slow, starting with one-half the usual adult dose or even less.

SSRIs (sertraline, citalopram, etc) are still the go-to class because they are safe and generally well tolerated. But in elderly patients tremors can occur, Parkinsonism, restlessness, akathisia, anorexia, weight gain, and falls. It is not recommended to take more than 20 mg/day of citalopram in patients over 60 as it increases the risk of QT prolongation and torsades.

SNRIs (venlafaxine, etc) are usually less well tolerated than SSRIs but should be considered in patients with neuropathic pain. Monitor BP, especially when the dose is increased. SNRIs can cause dose-dependent diastolic hypertension. SNRIs can also negatively impact lipids so lipid profiles need to be watched.

Mirtazapine (*Remeron*, etc) is another second-line option considered for elderly patients who need help with insomnia, agitation, or restlessness and also for patients who are losing too much weight. However evidence supporting weight gain is scant. It is best taken in the evening to avoid daytime sedation.

Trazodone is often tried for insomnia in low doses. But other options are suggested first for depression. At the higher depression doses, orthostatic hypotension and excessive sedation can be a problem.
Tricyclics such as desipramine and nortriptyline are usually best saved for older patients with neuropathic pain who don't get relief from other options. Their anticholinergic burden should be closely watched to avoid cognitive decline and other side effects. This should be used cautiously in patients with BPH, urinary retention, confusion, or heart disease.

Source: PharmacistLetter.com

Shortages continued from Page 1

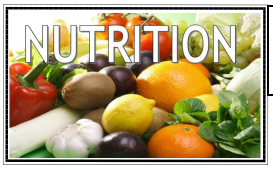
When the US manufacturers are not able to resolve a shortage immediately and the shortage involves a critical drug needed for US patients, FDA searches for overseas companies that are willing and able to import the drug until the shortage is resolved. FDA evaluates the overseas drug to ensure that it is of adequate quality and that the drug does not pose significant risks for US patients. The information about the imported drug and how patients can access supplies is posted on the FDA Drug Shortage website along with the Dear Healthcare Professional letter from the company that is importing the drug. FDA cannot always find a company willing and able to import a drug during a shortage; however, it is something we explore when there is a critical shortage and US patient needs are not being met.

FDA works to find ways to mitigate drug shortages; however, there are a number of factors that can cause or contribute to drugs shortages that are outside of the control of FDA. It's important to note that not all shortages can be prevented. Natural disasters, severe quality defects, or unforeseen manufacturing shutdowns are examples of situations where a shortage may not be able to be prevented.

FDA works to communicate information about shortages based on information provided by the manufacturers and learned through reports from health care professionals. Companies voluntarily provide the shortage information posted on the FDA website. They are required to report shortages of sole source, medically necessary drugs, but there are no penalties for failure to report. Manufacturers are not required to report information about disruptions in drug supplies to FDA, and are not required to always report the reasons for disruptions or the expected duration of shortages on the FDA website.

Problems can and do occur at any point in the manufacturing process and the manufacturing of sterile injectables is particularly complex and involves many steps where things can go wrong. When problems occur at any step in the process, FDA encourages companies to notify FDA of any potential supply issues so we can help address the problem.

Source: Medscape.com



UPDATE

"For years there has been heated debates within the medical community about supplements helping to reduce the risk of certain diseases, but scientific studies have repeatedly failed to support these claims," says Dr. Arthur Agatston, preventive cardiologist and author of *The South Beach Diet*® and *The South Beach Heart Health Revolution*.

The disappointing results of studies on vitamin supplements and their purported health benefits come as no surprise to Dr. Agatston: "I've been following the scientific evidence closely for many years and have always understood that supplements are not the magic bullet for improving health or preventing disease — eating a good variety of vegetables and fruits, along with healthy fats, such as omega-3s and olive oil, is still the optimal way to get the natural vitamins and nutrients that prevent heart attacks, strokes, cancers, and other chronic diseases."

That said, research has shown that one supplement will make a difference: fish oil. Study after study — including the landmark GISSI-Prevention Study, which found that a daily dose of fish oil substantially decreased the risk of sudden death in heart-attack survivors — consistently demonstrates that fish oil helps prevent and treat cardiovascular disease, decreases sudden death from heart attack, and may even stave off Alzheimer's disease.

In addition, fish oil, which contains two omega-3 fatty acids, eicosapentaenoic and docosahexaenoic acids (EPA and DHA), has been shown to reduce the inflammation that is a predictor of heart disease — and that's a result which may help avert the risk of deadly heart attacks or strokes. "A certain amount of inflammation in the body is good because it helps blood to clot and wards off infection," explains Dr. Agatston. "But too much inflammation may cause plaque in the arteries to rupture, leading to a blood clot that could cause a heart attack or stroke. To prevent cardiovascular disease and minimize dangerous levels of inflammation in the body, the one supplement that adult men and women should be taking is fish oil."

Source: Everydayhealth.com